Proliferation inhibition activity of vitamin E to "activated" hepatic stellate cells, which participate the principal function in liver fibrosis and liver cirrhosis

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Hepatic stellate cells are localized in sinusoidal space of liver. In pathological conditions, such as liver fibrosis or liver cirrhosis, they lose lipid droplets, morphologically change to myofibroblast-like phenotype and acquire increased proliferation activity. They also become synthesizing relatively large amount of matrix components including fibrillar collagens, what is called the "activated" state. Vitamin E is composed of eight different forms: α-, β-, γ-, and δ-tocopherols and α-, β-, γ- and δ-tocotrienols. Tocol is lacking methyl groups attached to the chromanol ring and considered to be a potential drug delivery vehicle for poorly soluble and watersoluble drugs. All vitamin E molecules are well known as antioxidants, however, recent research developments demonstrated that they possess powerful cholesterol lowering, platelet adhesion inhibition and anti-cancer properties.

We have investigated the treatment for liver fibrosis based on the concept of targeting "activated" hepatic stellate cells by introducing "non-activated" condition. In this study, four tocopherols and tocol were applied to "activated" hepatic stellate cells and examined the effects on proliferation activity of stellate cells. Rat hepatic stellate cells were prepared by collagenase perfusion and the "activated" state was induced by culture in vitro and passage once. Among four tocopherols and tocol, relatively high proliferation inhibition effects were detected in δ-tocopherol and tocol. In addition to proliferation inhibition, cell detachment and apoptosis were observed in tocol treated cells in a dose response manner. These data suggest that vitamin E is effective for the treatment of hepatic fibrosis and liver cirrhosis.